UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte HYAM I. LEVITSKY and IVAN BORRELLO

Appeal No. 2005-1336
Application No. 09/992,443

ON BRIEF

Before ADAMS, GRIMES, and GREEN, Administrative Patent Judges.

GREEN, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-14, 17-28, 40-47 and 50-53. Claim 1 is representative of the subject matter on appeal, and reads as follows:

1. A universal bystander human cell line, which:
(i) is a human cell line,
(ii) naturally lacks major histocompatibility class I (MHC-I) antigens and major histocompatibility class II (MHC-II) antigens, and
(iii) is modified by introduction of a nucleic acid molecule comprising a nucleic acid sequence encoding granulocyte macrophage-colony stimulating factor (GM-CSF) operably linked to a promoter,
wherein said universal bystander cell line expresses about 500 ng or greater GM-CSF/10^6 cells/24 hours.

Claims 1-3, 5-7, 9-12, 17, 19, 20, 22-28, 40, 41, 44-47, 50 and 52 stand rejected under 35 U.S.C. §112, first paragraph, as lacking written description.[1] Those claims also stand rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. In addition, claims 1-14, 17-28, 40-47 and 50-53 stand rejected under the judicially created doctrine of obviousness-type double patenting. After careful review of the record and consideration of the issues before us, we affirm the rejection under 35 U.S.C. § 112, first paragraph, as well as the obviousness-type double patenting rejection. Because we have affirmed the rejection of claims 1-3, 5-7, 9-12, 17, 19, 20, 22-28, 40, 41, 44-47, 50 and 52 under 35 U.S.C. §112, first paragraph, as lacking written description, we decline to reach the merits of the rejection under 35 U.S.C. § 112, first paragraph, for lack of enablement.

BACKGROUND

"Cancer immunotherapy is a therapeutic treatment of cancer. It is based on the premise that the failure of the immune system to reject spontaneously arising tumors is related to the failure of the immune system to respond appropriately to tumor antigens." Specification, page 1.

"Active immunotherapy involves the injection of cancer or tumor cells to generate either a novel or an enhanced systemic immune response. The tumor cells employed can be autologous, i.e., derived from the host to be treated, or

[1] The examiner withdrew the rejection of claims 4, 8, 13, 14, 18, 21, 42, 43, 46, 51 and 53 under 35 U.S.C. §112, as lacking written description and enablement, as well as the rejections under 35 U.S.C. §112, second paragraph, and 35 U.S.C. §103(a), in the Examiner's Answer. Id. at 4.

allogeneic, i.e., derived from a host other than the one to be treated. Such a strategy is referred to as a 'vaccine,' meaning use of an antigen source, such as an intact cancer or tumor cell, to stimulate an immune response against established metastatic cancer—not prophylactic immunization." Id. at 1-2.

According to the specification:

> The present invention provides a universal immunomodulatory cytokine-expressing bystander cell line. The universal bystander cell line is a human cell line, which either naturally lacks major histocompatibility class I (MHC-I) antigens and major histocompatibility class II (MHC-II) antigens or is modified so that it lacks MHC-I antigens and MHC-II antigens. In addition, the universal bystander cell line is modified by introduction of a nucleic acid molecule comprising a nucleic acid sequence encoding an immunomodulatory cytokine operably linked to a promoter. Preferably, the immunomodulatory cytokine is granulocyte macrophage-colony stimulating factor (GM-CSF).

Id. at 5.

With respect to cell lines that naturally lack MHC-I antigens and MHC-II antigens, the specification teaches that "[a] preferred human cell line is one that is derived from a blast crisis of chronic myeloid leukemia. An example of a preferred cell line is K562." Id. at 5; see also id. at 7, 18.

DISCUSSION

1. Written Description

Initially we note that the claims stand or fall together for each ground of rejection, thus we focus our analysis on representative claim 1. See Appeal Brief, page 4. In addition, we did not consider appellants' Reply Brief, filed

January 31, 2005, as that brief was not entered by the examiner. See Office Communication, mailed April 19, 2005.

Claims 1-3, 5-7, 9-12, 17, 19, 20, 22-28, 40, 41, 44-47, 50 and 52 stand rejected under 35 U.S.C. §112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.[2]

According to the examiner, "[t]he standing claims are rejected because the specification fails to provide an adequate written description for the starting materials necessary to make the claimed genus of genetically modified universal bystander human cell lines expressing GM-CSF." Examiner's Answer, page 6 (emphasis in original).

The examiner interprets "naturally" as "cell lines that never had MHC-I and MHC-II antigens, and cell lines that lost MHC-I and MHC-II antigens due to cancerous mutation." Id. at 6. The examiner notes that all nucleated cells naturally and constitutively express MHC-I antigens, and immune system cells express MHC-II antigens. See id. at 6-7. Therefore, the examiner concludes that the only cell line that meets the limitation of a cell line that never had MHC-I and MHC-II antigens are red blood cells, and that the specification fails to describe a red blood cell line that, since it is lacking a nucleus, is also modified to express GM-CSF. See id. at 7-8. With respect to those cell lines that have

[2] The rejection of claims 4, 8, 13, 14, 18, 21, 42, 43, 46, 51 and 53 was withdrawn by the examiner "because these claims are drawn to a specific human cell line K562, and methods of making and using such, which relates to the subject matter claimed in U.S. patent 6,464,973." Examiner's Answer, page 6.

lost MHC-I and MHC-II antigens due to a cancerous mutation, the examiner notes that the only such cell line described by the specification is the K562 cell line derived from a patient with blast crisis of chronic myeloid leukemia. See id. at 8. The examiner goes on to state that "out of hundreds if not thousands of tumor cell lines, for which the surface markers may extremely vary and new mutations constantly occur, K562 is the only cell line, disclosed by the appellant either in the specification or in the subsequently submitted references, proven to be lacking both MHC-I And MHC-II antigens. In view of such, the disclosure fails to provide a representative species for the claimed genus, i.e., human cell lines that never had or lost MHC-I and MHC-II antigens." Id. at 8 (emphasis in original).

In Enzo Biochem, Inc. v. Gen-Probe Inc., 323 F.3d 956, 63 USPQ2d 1609 (Fed. Cir. 2002), the Federal Circuit adopted a portion of the Guidelines proffered by the United States Patent and Trademark Office (USPTO). The court stated that:

> [T]he written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of characteristics."

Enzo Biochem, 323 F.3d at 964, 63 USPQ2d at 1613 (citing Guidelines for Examination of Patent Applications Under the 35 U.S.C. § 112, ¶ 1 "Written Description" Requirement, 66 Fed. Reg. 1099, 1106 (January 5, 2001)).

In University of Rochester v. G.D. Searle & Co., Inc., 358 F.3d 916, 69 USPQ2d 1886, (Fed. Cir. 2004), the Court of Appeals for the Federal Circuit held that claims drawn to methods of inhibiting PGHS-2 activity by administering a non-steroidal compound that inhibits activity of prostaglandin H synthase-2 were invalid for failing to comply with the written description requirement of 35 U.S.C. § 112, first paragraph. See 358 F.2d at 917-18, 69 USPQ2d at 1887-88.

The University of Rochester court made clear that cases such as Enzo do not apply only to claims to genetic material, as the written description requirement applies to all types of inventions. See 358 F.2d at 925, 69 USPQ2d at 1893-94. Moreover, while disclosure of a DNA sequence may support claims to complementary molecules that can hybridize to it due to the complementarity of genetic material, "[t]he same is not necessarily true in the chemical arts more generally." See id. Thus, "[a] description of what a material does, rather than of what it is, usually does not suffice." See 358 F.2d at 923, 69 USPQ2d at 1892 (citation omitted).

Whether the level of disclosure in the specification would have allowed one skilled in the art to recognize that the inventor invented what is claimed is a question of fact. The USPTO has summarized a number of factors to be considered in making this determination; they include "the level of skill and knowledge in the art, partial structure, physical and/or chemical properties,

functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention." Guidelines for Examination of Patent applications under the 35 U.S.C. § 112, ¶ 1, "Written Description" Requirement, 66 Fed. Reg. 1099, 1106 (Jan. 5, 2001). "Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." Id.

In the case before us, as noted by the examiner, the only cell line described by the disclosure as filed, that naturally lacks MHC-I and MHC-II antigens as required by claim 1, is the K562 cell line. As the specification does not set forth a partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function for additional cell lines that naturally lack MHC-I and MHC-II antigens, we agree with the examiner that the disclosure as filed fails to adequately describe the genus of human cell lines that naturally lack MHC-I and MHC-II antigens as required by claim 1, and the rejection is affirmed.

Appellants argue that the specification teaches the K562 cell line, which lacks MHC-I and MHC-II antigens, and cite Wang (1993),[3] Ferrone,[4] Kageshita[5] and Wang (1996),[6] as examples of cell lines known in the art prior to the February 2, 1998, priority date, to lack MHC-I and MHC-II antigens. See Appeal Brief, page 6. Appellants' arguments are not convincing. We agree that the specification describes the K562 cell line. That cell line is, however, as discussed above, the only cell line that lacks both MHC-I and MHC-II antigens described by the specification. And as also noted above, the specification does not set forth a partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function so as to adequately describe additional cell lines that naturally lack MHC-I and MHC-II antigens.

Moreover, with respect to the Wang (1993), Ferrone, Kageshita and Wang (1996) references, as noted by the examiner, those references teach cell

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[3] Wang et al. (Wang (1993)), "Lack of HLA Class I Antigen Expression by Melanoma Cells SK-MEL-33 Caused by a Reading Frameshift in β_2-Microglobulin Messenger RNA," J. Clin. Invest., Vol. 9, pp. 684-692 (1993).

[4] Ferrone et al. (Ferrone), "Loss of HLA class I antigens by melanoma cells: molecular mechanisms, functional significance and clinical relevance," Immunology Today, Vol. 16, pp. 487-494 (1995).

[5] Kagashita et al. (Kagashita), "Selective Loss of Human Leukocyte Class I Allospecificities and Staining of Melanoma Cells by Monoclonal Antibodies Recognizing Monomorphic Determinants of Class I Human Leukocytic antigens," Cancer Research, Vol. 53, pp. 3349-3354 (1993).

[6] Wang et al. (Wang 1996), "Molecular and functional phenotypes of melanoma cells with abnormalities in HLA Class I antigen expression," Tissue Antigens, Vol. 47, pp. 382-390 (1996).

lines that naturally lost the MHC-I antigen to cancerous mutation, but do not teach "a cell line that [is] confirmed lacking both MHC-I and MHC-II antigens." Examiner's Answer, page 16. See the examiner's extended analysis, pages 16-19 of the Examiner's Answer, which cites Winchester,[7] that demonstrates that the references cited by appellants do not provide support for appellants' assertion that the prior art provides examples of cell lines that naturally lack both MHC-I and MHC-II antigens as required by claim 1.

Appellants argue further that the specification teaches the use of antibodies to determine whether a cell line expresses MHC-I and MHC-II antigens, and thus "[w]hether or not a given cell line naturally lacks MHC-I and MHC-II antigens is readily ascertainable – either the human cell line expresses MHC-I and/or MHC-II or it does not." Appeal Brief, page 7. Appellants also assert that that database searching and routine screening, "even if on a 'large-scale' basis, do not constitute undue experimentation." Id.

Appellants' arguments are not convincing, as they are directed to enablement and not written description. As noted by the Court of Appeals for the Federal Circuit, our reviewing court, however, the requirement for written description under the first paragraph of section 112 is separate and distinct from the enablement requirement of that paragraph. See Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1116-17 (Fed. Cir. 1991). We also

[7] Winchester et al. (Winchester), "Expression of Ia-like antigens on cultured human malignant melanoma cell lines," Proc. Natl. Acad. Sci. USA, Vol. 75, pp. 6235-6239 (1978).

note appellants' proposed amendment to claim 1 presented on page 8 of the Appeal Brief. That amendment, however, should first be presented to the examiner, and we decline to comment on the amendment here.

2. Obviousness-Type Double Patenting

Claims 1-14, 17-28, 40-47 and 50-53 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-21 of U.S. Patent No. 6,464,973.[8]

Appellants do not argue the merits of the rejection, but merely state that "[u]pon an indication of allowable subject matter, Appellants will submit a terminal disclaimer, which will render this rejection moot." Appeal Brief, page 14. As such, this rejection is summarily affirmed.

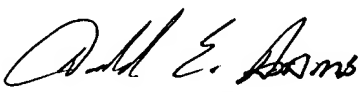
CONCLUSION

The rejection of claims 1-3, 5-7, 9-12, 17, 19, 20, 22-28, 40, 41, 44-47, 50 and 52 under 35 U.S.C. §112, first paragraph, as lacking written description, is affirmed. We also affirm the obviousness-type double patenting rejection. Because we have affirmed the rejection of claims 1-3, 5-7, 9-12, 17, 19, 20, 22-28, 40, 41, 44-47, 50 and 52 under 35 U.S.C. §112, first paragraph, as lacking written description, we decline to reach the merits of the rejection under 35 U.S.C. § 112, first paragraph, for lack of enablement.

[8] Levitsky et al., issued October 15, 2002.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136 (a).

AFFIRMED



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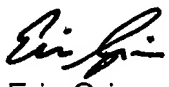
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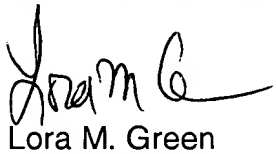
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